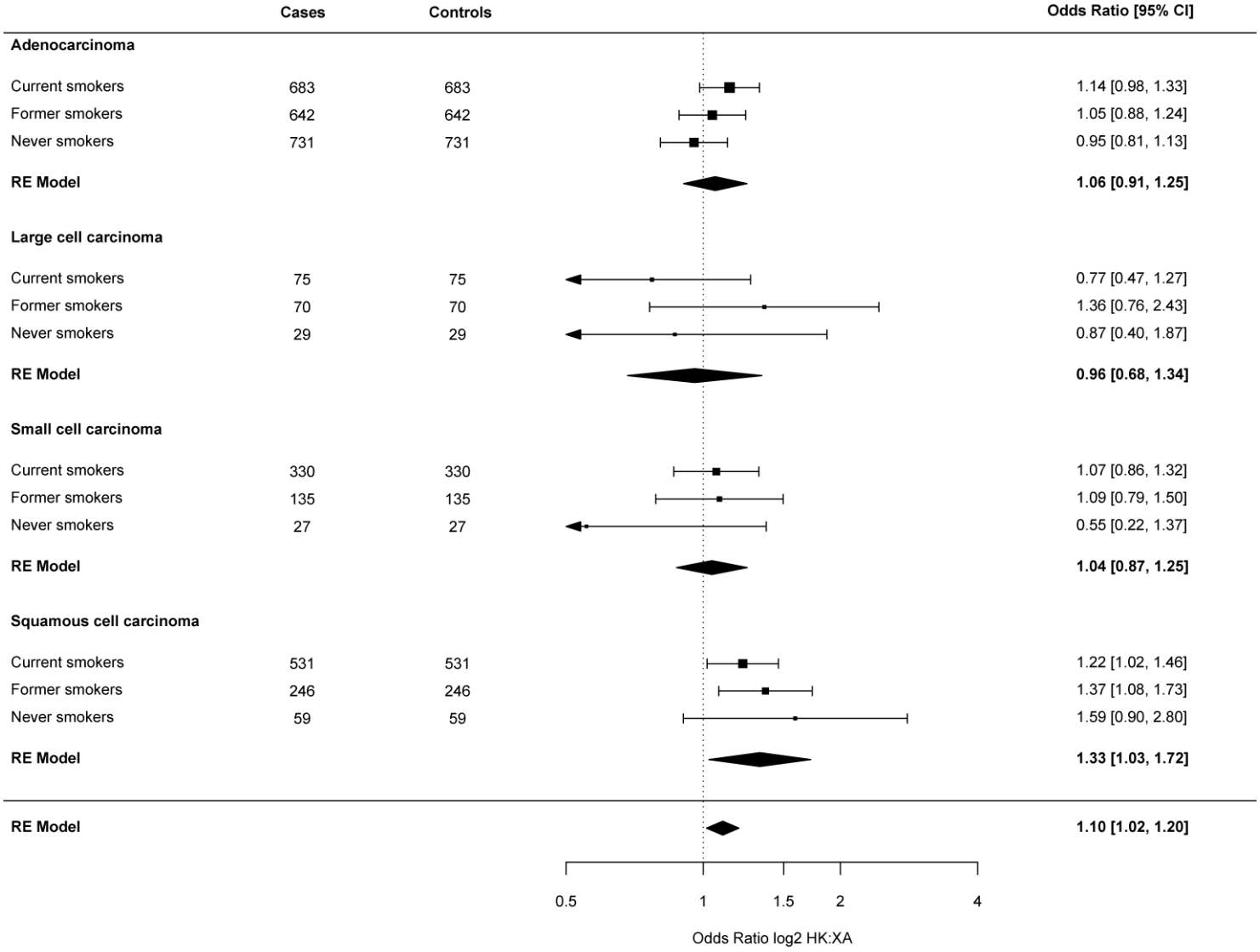
Theofylaktopoulou, D., Midttun, Ø., Ueland, P. M., Meyer, K., Fanidi, A., Zheng, W., Shu, X. O., Xiang, Y. B., Prentice, R., Pettinger, M., Thomson, C. A., Giles, G. G., Hodge, A., Cai, Q., Blot, W. J., Wu, J., Johansson, M., Hultdin, J., Grankvist, K., ... Ulvik, A. (2018). Impaired functional vitamin B6 status is associated with increased risk of lung cancer. *International Journal of Cancer*, *142*(12), 2425-2434. https://doi.org/10.1002/ijc.31215

Peer reviewed version

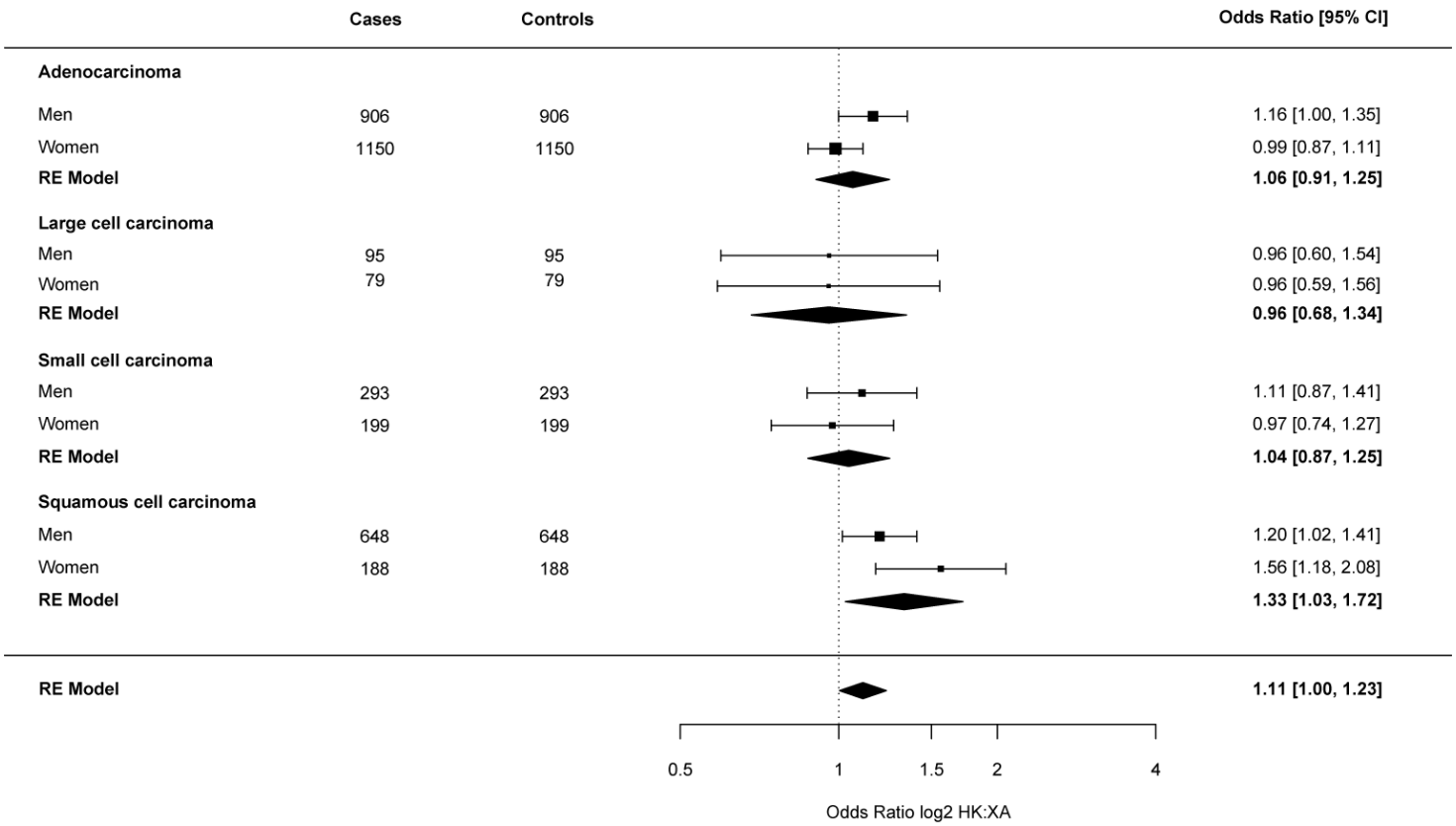
Link to published version (if available):
10.1002/ijc.31215

SUPPLEMENTARY MATERIAL



Supplemental Figure S1. Forestplot showing odds ratios for different types of lung cancer for a log2 increase of HK:XA stratified by smoking status.

Conditional logistic regression was performed for each subgroup and was adjusted for smoking intensity using quartiles of cotinine among current smokers. Cases and controls were matched on age, sex, and smoking status. Results were combined using random effect models. HK:XA, 3-hydroxykynurenine/xanthurenic acid.



Supplemental Figure S2. Forestplot showing odds ratios for different types of lung cancer for a log2 increase of HK:XA stratified by sex.

Conditional logistic regression was performed for each subgroup and was adjusted for smoking intensity using quartiles of cotinine among current smokers. Cases and controls were matched on age, sex, and smoking status. Results were combined using random effect models. HK:XA, 3-hydroxykynurenine/xanthurenic acid.

Supplemental Table S1. Heterogeneity for risk of lung cancer across cohorts, by region.

Region	I^2 (%)	Q test		
		Q value	df	p-value
All	7.1	23.5	19	0.22
USA	31.7	15.5	10	0.12
Europe	7.3	3.2	3	0.37
Asia	0.0	2.3	3	0.51

Supplemental Table S2. Odds ratio across quartiles of HK:XA in the different regions.

	Range	Cases/ Controls	Total Crude	Total (adj)*	Never smokers	Former smokers	Current smokers*	Men *	Women *
	Asia								
1	(0.04 - 2.27)	399 / 431	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
2	(2.27 - 3.01)	417 / 430	1.07 (0.88 ; 1.30)	1.05 (0.86 ; 1.28)	1.35 (0.98 ; 1.88)	1.14 (0.63 ; 2.04)	0.84 (0.64 ; 1.11)	1.11 (0.69 ; 1.79)	1.45 (1.02 ; 2.07)
3	(3.01 - 4.11)	419 / 430	1.08 (0.89 ; 1.32)	1.04 (0.85 ; 1.27)	0.91 (0.65 ; 1.28)	1.13 (0.62 ; 2.05)	1.10 (0.83 ; 1.46)	0.95 (0.57 ; 1.58)	0.97 (0.67 ; 1.39)
4	> 4.11	487 / 430	1.28 (1.04 ; 1.57)	1.18 (0.95 ; 1.46)	0.84 (0.59 ; 1.20)	1.81 (0.92 ; 3.56)	1.29 (0.97 ; 1.73)	0.93 (0.53 ; 1.60)	1.04 (0.71 ; 1.54)
	P for trend		0.03	0.15	0.14	0.12	0.02	0.67	0.67
	Australia								
1	(0.35-2.21)	89 / 89	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
2	(2.21-2.87)	69 / 88	0.79 (0.50 ; 1.26)	0.82 (0.51 ; 1.31)	0.35 (0.07 ; 1.79)	1.21 (0.59 ; 2.49)	0.68 (0.33 ; 1.38)	1.14 (0.48 ; 2.67)	0.68 (0.23 ; 1.99)
3	(2.88-3.97)	97 / 88	1.13 (0.71 ; 1.79)	1.14 (0.72 ; 1.82)	0.60 (0.16 ; 2.30)	1.74 (0.87 ; 3.51)	0.83 (0.40 ; 1.75)	1.83 (0.74 ; 4.52)	1.02 (0.40 ; 2.56)
4	>3.97	99 / 89	1.14 (0.72 ; 1.80)	1.15 (0.72 ; 1.83)	0.77 (0.19 ; 3.13)	1.23 (0.59 ; 2.54)	1.06 (0.52 ; 2.15)	2.64 (1.00 ; 6.96)	0.52 (0.21 ; 1.30)
	P for trend		0.29	0.29	0.53	0.44	0.59	0.033	0.25
	Europe								
1	(0.94 - 2.22)	148 / 209	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
2	(2.23 - 3.08)	222 / 209	1.56 (1.17 ; 2.07)	1.53 (1.14 ; 2.05)	1.19 (0.64 ; 2.24)	1.24 (0.69 ; 2.22)	1.85 (1.23 ; 2.77)	1.18 (0.64 ; 2.14)	1.50 (0.80 ; 2.82)
3	(3.08 - 4.28)	212 / 208	1.52 (1.13 ; 2.04)	1.42 (1.05 ; 1.92)	1.23 (0.56 ; 2.67)	1.33 (0.75 ; 2.38)	1.58 (1.05 ; 2.37)	1.67 (0.80 ; 3.51)	1.10 (0.59 ; 2.03)
4	> 4.28	251 / 209	1.90 (1.39 ; 2.59)	1.73 (1.26 ; 2.38)	1.06 (0.40 ; 2.82)	2.33 (1.23 ; 4.39)	1.73 (1.14 ; 2.63)	1.95 (0.85 ; 4.45)	1.82 (0.92 ; 3.63)
	P for trend		<0.001	0.002	0.76	0.01	0.037	0.07	0.22
	USA								
1	(0.31 - 2.10)	547 / 599	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
2	(2.11 - 2.93)	556 / 599	1.04 (0.88 ; 1.22)	1.03 (0.87 ; 1.22)	0.92 (0.64 ; 1.34)	1.01 (0.79 ; 1.29)	1.14 (0.85 ; 1.51)	1.10 (0.81 ; 1.50)	0.89 (0.67 ; 1.18)
3	(2.93 - 4.26)	615 / 598	1.16 (0.98 ; 1.38)	1.15 (0.96 ; 1.36)	1.22 (0.84 ; 1.76)	1.07 (0.83 ; 1.38)	1.18 (0.87 ; 1.59)	1.22 (0.88 ; 1.70)	1.04 (0.79 ; 1.38)
4	> 4.26	678 / 599	1.30 (1.09 ; 1.55)	1.29 (1.08 ; 1.55)	1.16 (0.80 ; 1.70)	1.23 (0.94 ; 1.61)	1.50 (1.10 ; 2.03)	1.69 (1.16 ; 2.45)	0.99 (0.75 ; 1.31)
	P for trend		0.001	0.002	0.23	0.12	0.01	0.008	0.87

Results are odds ratio (95%confidence interval) from conditional logistic regression. Cases and controls were matched on age, sex, and smoking status.

* Adjusted for smoking intensity using quartiles of cotinine among smokers

HK:XA, 3-hydroxykynurenine/xanthurenic acid

Supplemental Table S3. Heterogeneity for risk of lung cancer by sex.

Sex	I^2 (%)	Q test		
		Q value	df	p-value
All	62.4	18.9	7	0.0084
Men	51.2	6.3	3	0.10
Women	73.6	9.0	3	0.029

Supplemental Table S4. Heterogeneity for risk of lung cancer by smoking status.

Smoking category	I^2 (%)	Q test		
		Q value	df	p-value
All	30.1	15.0	11	0.18
Current smokers	0.0	3.4	3	0.33
Former smokers	20.0	3.5	3	0.32
Never smokers	12.7	2.2	3	0.54